

# Risk Factors for Asthma up to 16 Years of Age\*

## Evidence from a National Cohort Study

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From a national cohort of 8,806 children examined at ages seven, 11 and 16 years (National Child Development Study), data on asthma or wheezing illness (AW) were analyzed to describe its natural history in childhood and its risk factors. Factors found to predict the subsequent onset of asthma included male sex of child, mother's age at the child's birth, pneumonia, whooping cough, tonsillectomy/adenoidectomy, allergic rhinitis, eczema and periodic abdominal pain/vomiting attacks. A wide range of perinatal factors, including smoking practices and social background factors, were found to have no effect on natural history.

Much of the existing epidemiologic evidence about the etiology of asthma rests on prevalence and follow-up studies and there is a serious lack of population-based cohort data. The National Child Development Study (NCDS) originated in the National Perinatal Study<sup>1</sup> and went on to become a multipurpose cohort study of child development including health. While it was not designed specifically to study the epidemiology of asthma, it is nevertheless possible to obtain valuable information relating to the natural history of asthma. This article describes some of the findings from our analysis of NCDS data which have implications for the etiology of asthma.

### MATERIALS AND METHODS

The NCDS followed-up at ages seven, 11 and 16 all children in England, Scotland and Wales born during one week of March, 1958. At each follow-up, information about current or past asthma or wheezing illness was obtained as part of a structured questionnaire on medical and other topics administered to parents by health visitors. The wording of the asthma questions varied at each interview but it was nevertheless possible to classify subjects at each interview into three categories: no asthma or wheezing, previous asthma or wheezing but not in the past 12 months, and current asthma or wheezing (symptoms reported in the past 12 months). Based on these three possibilities at each of three interviews, 27 mutually exclusive natural history categories can be created. Some of these contain small numbers or are of limited clinical or epidemiologic interest, and so for the purpose of the present analysis a collapsed classification of six natural history categories was used.

These natural history categories were analyzed in relation to medical and social data collected at each of the follow-up medical examinations and home interviews. Factors that have previously been reported to be associated with asthma or wheezing were selected together with those considered likely to influence the natural history of asthma.

The overall association between a variable and the natural history category was tested using the Chi-squared test or one-way analysis of variance as appropriate. Where there was a statistically significant

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Table 1—Lifetime Incidence of Asthma or Wheezing (n = 8,806)

Age at interview (yrs)	Asthma or wheezing at any time in past (percent)	
	Cross-sectional	Cumulative*
7	18.3	18.3
11	12.1	21.9
16	11.6	24.7

\*Using information from previous interviews

Table 2—Prevalence of Asthma or Wheezing in 12 Months Preceding Interview (n = 8,806)

Age at interview (yrs)	Asthma or Wheezing in past 12 months (percent)	
	Cross-sectional	Cumulative*
7	8.3	8.3
11	4.7	10.7
16	3.5	11.1

\*Using information from previous interviews

overall association, the relative risks of each natural history category were calculated. The statistical significance of the relative risk was tested by calculating 95 percent confidence intervals.

### RESULTS

Data on asthma or wheezing were obtained at all three ages for 8,806 of the original NCDS cohort of over 15,000 children living in England, Scotland and Wales and available for follow-up at seven years.

The reported lifetime incidence of asthma or wheezing is shown in Table 1. Using data from all three interviews, a total of 24.7 percent of children had experienced asthma or wheeze by the age of 16 years. When questioned at age 16 years, however, the proportion reporting past asthma or wheeze was less than half this figure (11.6 percent). The prev-

Table 3—Prognosis of Asthma or Wheezing if Current (past 12 months) at Age 7 (n = 731)

Persistence of AW and age (yrs)	Percent of 7-year-olds who reported current AW
Current at 11	28.3
Current at 16	16.3
Current at 11 and 16	10.5
Current at 11 or 16	34.1
Not current at 11 or 16	65.9

Table 4—Natural History Categories (n = 8,806)

Category	Percent of sample
Never had asthma or wheezing	75.3
Onset before age 7 but not current at 7 or reported subsequently	8.6
Current at age 7 but not reported subsequently	5.5
Onset age 0 to 7 and also reported at 11 or 16	4.2
Onset age 8 to 11	3.6
Onset age 12 to 16	2.8

Table 5—Factors Predicting the Onset of Asthma or Wheezing

Predictive factors	Overall $\chi^2$ P value	Relative risk of:	Natural history				
			By age 7 not after	At age 7 not after	Age 0-7 and after	Age 8-11 onset	Age 12-16 onset
Perinatal							
Sex of child	<0.001	Boy: girl	1.1	1.2	1.4*	1.3*	1.4*
Mother's age	<0.001	15-19: 20-29 yrs	1.4*	1.5*	1.1	1.9*	1.7*
		15-19: 30+ yrs	1.6*	1.3	1.3	1.9*	2.0*
		20-29: 30+ yrs	1.2	0.9	1.1	1.0	1.2
		Smoking in pregnancy	<0.001	Smoker: Non-smoker	1.3*	1.2	0.8
Region of child's birth	<0.01	North: Centre	0.7*	0.9	0.9	0.7	1.0
		North: South	0.8*	0.9	1.0	0.9	1.0
		Centre: South	1.1	1.0	1.0	1.2	1.0
Assessed at 7							
History of pneumonia	<0.001	Yes: No	2.0*	2.0*	4.3*	1.5	1.8*
Tonsillectomy/ adenoidectomy	<0.001	Yes: No	1.3*	1.2	1.2	1.2	1.4*
Eczema in 1st year	<0.001	Yes: No	1.2	1.4	5.4*	1.7*	1.5
Eczema after 1st year	<0.001	Yes: No	1.1	1.3	4.7*	1.3	1.7*
Eczema on Dr. exam.	<0.001	Yes: No	0.8	1.1	4.9*	1.6	2.1*
Hayfever or sneezing ever	<0.001	Yes: No	1.3	2.0*	7.1*	1.5	1.7*
Periodic vomiting or bilious attacks ever	<0.001	Yes: No	1.2*	1.4*	1.8*	0.8	1.4*
Periodic abdominal pain ever	<0.001	Yes: No	1.4*	1.3*	1.5*	0.9	1.4*
Assessed at 11							
Whooping cough ever	<0.001	Yes: No	1.2*	1.3*	1.4*	1.4*	1.4*
Eczema in past year	<0.001	Yes: No	1.2	1.2	4.2*	1.9*	1.7*
Hayfever or allergic rhinitis in past year	<0.001	Yes: No	1.0	1.2	5.2	2.2*	1.9*

\*P&lt;0.05

absence of current asthma was highest at seven years (8.3 percent) but had fallen to 3.5 percent at 16 years (Table 2). At each interview, the lifetime and current rates for the present cohort (those with data available at all interviews) were similar to those among subjects interviewed only once or twice. Of those with current symptoms at seven, 28 percent reported current symptoms at 11 years, 16 percent at 16 years and 11 percent at both ages (Table 3).

For the purpose of analysis, the 27 patterns of questionnaire response were collapsed into the six categories described in Table 4.

From an etiologic standpoint two types of relationship could be discerned. In the first, a given factor was assessed prior to the onset of asthma or wheeze, and could therefore be considered predictive. In the other, the order of occurrence of the factor and the onset of asthma or wheezing could not, from the data available, be shown to be predictive because the assessment of both factors was concurrent. Most factors found to be predictive are shown in Table 5 together with their relative risks. Any concurrent associations for these variables are also shown. Of the perinatal factors the most prominent was sex of the child and the mother's age at birth of the child. Multifactorial analysis was done to explore whether social class or breast feeding might explain this latter relationship, but this was not the case.

Of the factors assessed at seven or 11 years, the main ones predicting subsequent onset of asthma or wheezing were atopic conditions—eczema or allergic rhinitis—and (at

seven years only) periodic vomiting or abdominal pain. A history of pneumonia (at seven years) and whooping cough (at 11 years) were also predictive. Previous tonsillectomy or adenoidectomy reported at age seven years predicted onset in adolescence (though not when reported at 11 years).

Those factors which were concurrently associated with asthma or wheezing but not predictive are shown in Table 6. They mainly comprise upper and lower respiratory conditions but also include fits or convulsions in the first year (but not continuing into later life), enuresis, headaches and one adverse socioeconomic factor—sharing of one or more household facilities.

Those factors not associated with natural history are listed in Table 7. Notably, these included breast feeding, social class and a variety of indicators of socioeconomic circumstances and family stress.

Assessment of smoking in the household was inadequate, available only for the mother while she was pregnant and for both parents when the child was 16 years old. Smoking in pregnancy was associated only with an increased relative risk of asthma or wheezing during the early years of life and smoking by one or both parents reported when the child was 16 years was not related. At 16 years, the child's own smoking habit was unrelated to the presence of asthma or wheezing.

#### DISCUSSION

The National Child Development Study was not designed to examine the etiology of asthma and there are a number of

Table 6—Factors Concurrently Associated with Asthma or Wheezing but not Predictive

Concurrent factors	Overall $\chi^2$ P value	Relative risk of:	Natural history				
			By 7 not after	At 7 not after	0-7 and after	8-11 onset	12-16 onset
Assessed at 7 yrs.							
Household facilities	<0.008	Shared: not shared	1.1	1.3*	0.9	1.0	0.8
Whooping cough ever	<0.001	Yes: No	1.4*	1.2	1.4*	1.2	1.3
Throat/ear infections with fever >3 in past yr	<0.001	Yes: No	1.2	1.6*	1.4*	0.7	1.0
Running ears ever	<0.001	Yes: No	1.3*	1.3	0.9	1.0	1.2
Fits or convulsions in 1st year	<0.001	Yes: No	1.2	1.8*	2.7*	1.0	0.6
Wet by day after 3 yrs	<0.004	Yes: No	1.2	1.7*	1.0	1.5	1.2
Wet by night after 5 yrs	<0.001	Yes: No	1.5*	1.2	1.0	1.2	1.1
Assessed at 11 yrs.							
Household facilities	<0.05	Shared: not shared	1.0	1.4*	1.1	0.8	1.1
Recurrent throat/ear infections in past yr treated by Dr	<0.001	Yes: No	1.1	1.0	1.5*	1.7*	1.1
Discharging ears in past year	<0.07	Yes: No	1.2	1.3	1.8*	1.6	0.7
Tonsils/adonoids removed	<0.001	Yes: No	1.2*	1.3*	1.2	1.2	1.0
Eczema on examination (Dr.)	<0.001	Yes: No	0.8	1.1	4.9*	1.6	2.1*
Recurrent headaches or migraine past year	<0.001	Yes: No	1.2	1.1	1.6*	1.2	1.1
Recurrent vomiting or bilious attacks in past year	<0.09	Yes: No	1.0	1.5*	1.3	1.5	1.0

\*P&lt;0.05

inadequacies in the nature and timing of both the assessment of asthma and wheezing and of etiologic factors. Against this is the advantage that these data relate to a national representative sample and contain a substantial number of subjects followed-up over a long time.

By including all children with reported asthma or wheezing, however mild, the present analysis may have missed associations that relate only to more severe asthma or wheezing, which is the main concern in medical practice. The data do, however, allow a simple grading of severity and this is being analyzed at present.

Considering the logistics of such a national cohort study, the response rate for information about asthma or wheezing on all three occasions of 59 percent of the original NCDS cohort could be judged as successful. Nevertheless, this raises the possibility of bias, which has been examined in detail.<sup>9</sup> It would appear that this is unlikely to have biased our results for relative risks or incidence and prevalence estimates. At any particular age, the prevalence rates among children for whom we had linked data were similar to the rates among those not seen on each occasion. The 12-month prevalence rates observed at age seven years were similar to those of other population surveys which have included all wheezing illnesses.<sup>10</sup>

As far as etiology is concerned, the most important findings in this study are those relating to factors which predicted or did not predict the later onset of asthma or wheezing. Among the perinatal factors, a new and possibly important finding was that the risk of all natural history categories apart from persistent asthma or wheezing (reported on all three

occasions) was increased in children of mothers who were under 20 years of age at the birth of the child. This was independent of social class or breast feeding (which were

Table 7—Factors Not Found to Be Predictive or Concurrently Associated with Asthma or Wheezing

<b>Perinatal</b>	
Birthweight	
Gestational age	
Parity	
Breast/bottle feeding	
Birth order	
Rank in family	
Social class	
<b>Assessed at 7</b>	
Crowding in household	
Number of children in household	
Tenure of accommodation	
Social class	
Separation from mother	
In local authority care	
Absence of one or more biological parents	
Previous measles	
<b>Assessed at 11</b>	
Previous measles	
Social class	
<b>Assessed at 16</b>	
Age at menarche	
Pubic hair rating (boys)	
Smoking of child	
Smoking of parents	